

**IN THE UNITED STATES DISTRICT COURT  
SOUTHERN DISTRICT OF NEW YORK**

SHIRE CANADA INC., SHIRE INTERNATIONAL  
LICENSING B.V., AND SHIRE US INC.,

Plaintiffs,

v.

BARR LABORATORIES, INC.,

Defendant.

09 Civ. 2380 (PGG) (KNF)

SHIRE CANADA INC., SHIRE INTERNATIONAL  
LICENSING B.V., AND SHIRE US INC.,

Plaintiffs,

v.

MYLAN INC., MYLAN PHARMACEUTICALS  
INC., AND MATRIX LABORATORIES LIMITED,

Defendants.

09 Civ. 2555 (PGG) (KNF)

SHIRE CANADA INC., SHIRE INTERNATIONAL  
LICENSING B.V., AND SHIRE US INC.,

Plaintiffs,

v.

NATCO PHARMA LIMITED,

Defendant.

09 Civ. 3165 (PGG) (KNF)

ECF CASE

**PLAINTIFFS' RESPONSIVE CLAIM CONSTRUCTION BRIEF**

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## I. INTRODUCTION

The unstated goal behind the claim construction positions Defendants advance is to so narrow the claims at issue that Defendants' proposed generic versions of Fosrenol® fall outside them. Defendants' proposals cannot be squared with the accepted canons of claim construction, and indeed are at odds with the testimony of their own experts.

The controlling rules of claim construction are well established. *First*, "words of a claim are generally given their ordinary and customary meaning." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (*en banc*) (internal quotation and citation omitted). *Second*, departure from ordinary meaning is warranted only if a "special definition . . . appears in the intrinsic record with reasonable clarity and precision." *DSW, Inc. v. Shoe Pavilion, Inc.*, 537 F.3d 1342, 1347 (Fed. Cir. 2008) (quoting *N. Telecom Ltd. v. Samsung Elecs. Co.*, 215 F.3d 1281, 1295 (Fed. Cir. 2000)). *Third*, "[i]t is improper for a court to add extraneous limitations to a claim, that is, limitations added wholly apart from any need to interpret what the patentee meant by particular words or phrases in the claim." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1325 (Fed. Cir. 2003) (quoting *Hoganas AB v. Dresser Indus., Inc.*, 9 F.3d 948, 950 (Fed. Cir. 1993)); *see, e.g., SRAM Corp. v. AD-II Eng'g, Inc.*, 465 F.3d 1351, 1358-59 (Fed. Cir. 2006).

Proper application of these canons require that Defendants' constructions be rejected and that the claims be construed consistent with their plain meaning, the specification, and prosecution history, as urged by Shire.

## II. THE '976 PATENT

### A. “Pharmaceutical Composition For The Treatment of Hyperphosphatemia” (Claim 1)

Term To Be Construed	Shire’s Proposal	Defendants’ Proposal
<b>pharmaceutical composition for the treatment of hyperphosphatemia</b>	therapeutic mixture ( <i>i.e.</i> , one which is sterile, reasonably safe and non-toxic) suitable for administration into the gastrointestinal tract for the treatment of hyperphosphatemia	a pharmaceutical composition wherein the amount of $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ present in the composition is effective to treat hyperphosphatemia

As Shire demonstrated in its opening brief, Defendants are not attempting to interpret the claim term here. Pls. Br. at 6-7. Defendants do not dispute that “pharmaceutical composition” has an ordinary and customary meaning in the art. Indeed, they use that very term in their proposed construction and offer no definition of it. To the extent that a construction of “pharmaceutical composition” would be helpful, Defendants express no disagreement with that offered by Shire based on the prosecution history, where the applicants elaborated upon the meaning of the term. Pls. Br. at 7-8; Brittain Decl. ¶¶ 73-74; Defs. Br. at 16.

Rather, Defendants improperly attempt to narrow the claim – under the pretext of interpretation – by baldly inserting a limitation foreign to it. Their proposed construction – “a pharmaceutical composition **wherein the amount of  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  present in the composition is effective to** treat hyperphosphatemia” – imposes a limitation on the amount of the recited crystalline forms in the claimed composition that is found nowhere in the claim. *See* Defs. Br. at 14-15. As the bolding in the text shows, Defendants have simply inserted an extra limitation into the existing claim language. That is not proper claim construction.

The Federal Circuit has admonished that “[i]t is improper for a court to add ‘extraneous’ limitations to a claim, that is, limitations added wholly apart from any need to interpret what the patentee meant by particular words or phrases in the claim.” *Amgen*, 314 F.3d at 1325 (internal

quotation marks omitted). “Absent a clear disavowal or contrary definition in the specification or the prosecution history, the patentee is entitled to the full scope of its claim language.” *Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004). There is no such disavowal or express definition in the specification or prosecution history, and Defendants do not argue otherwise.

The Federal Circuit rejected a similar attempt to add an unrecited amount requirement in *Northern Telecom Ltd. v. Samsung Electronics Co.*, 215 F.3d 1281 (Fed. Cir. 2000). There, the defendant proposed inserting the word “layer” into the construction of “etching of aluminum” to “ensure that only larger (i.e., non-‘trace’) quantities of etched aluminum” were covered by the claims. *Id.* at 1290. The Federal Circuit rejected such a construction, cautioning, “[n]ot only is the term ‘layer’ not found in claim 1, but neither is a limitation that establishes a minimum quantity of aluminum that must be etched to meet the claim. This court has repeatedly and clearly held that it will not read unstated limitations into claim language.” *Id.* (citations omitted).

Defendants’ improper attempt to add an amount limitation into Claim 1 is also contradicted by the language of other claims. The Federal Circuit has instructed that “when a patent claim does not contain a certain limitation and another claim does, that limitation cannot be read into the former claim.” *Amgen*, 314 F.3d at 1326 (internal quotation marks omitted); *see also Phillips*, 415 F.3d at 1314 (“Differences among claims can also be a useful guide in understanding the meaning of particular claim terms.”). Here, Claim 7 contains an explicit limitation on the amount of the specified lanthanum carbonate hydrate that must be used.<sup>1</sup> The fact that Claim 1 does not contain similar language indicates that, in contrast to Claim 7, it does

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<sup>1</sup> Claim 7 recites “administering to said subject **an amount** of lanthanum carbonate of the formula  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  wherein x has a value from 3 to 6 **effective to treat** said hyperphosphataemia.” JA 8 (emphasis added).

not require a particular amount of lanthanum carbonate hydrate to be present. *See, e.g., Kara Tech., Inc. v. Stamps.com, Inc.*, 582 F.3d 1341, 1347 (Fed. Cir. 2009) (finding error in a claim construction requiring use of a key because “when the inventor wanted to restrict the claims to require the use of a key, he did so explicitly,” and “[n]one of the claims at issue on appeal recite the term ‘key’”); *see also Voda v. Cordis Corp.*, 536 F.3d 1311, 1320 (Fed. Cir. 2008).

The specification provides no support for Defendants’ position, much less a clear statement justifying departure from the ordinary meaning of “pharmaceutical composition.” The first passage Defendants cite, Column 1, lines 53-58 (JA 6) (*see* Defs. Br. at 15) says nothing about the amount of lanthanum carbonate of the formula  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  in a composition. The other passage, Column 1, lines 64-67 (JA 6), concerns the method of treatment recited in Claim 7, not the composition recited in Claim 1. That passage states “[t]he invention may also be expressed *as a method of treating hyperphosphatemia . . .* comprising the administration of an effective dose of said lanthanum carbonate into the gastrointestinal tract. JA 6 (emphasis added). This tracks the express language of Claim 7 – which recites a method of treating hyperphosphatemia using an effective dose of lanthanum carbonate hydrate – and hence emphasizes the lack of such a limitation in Claim 1, which contains no such language. Certainly, it provides no warrant for adding a limitation to Claim 1 not found there. *See, e.g., Amgen*, 314 F.3d at 1325 (holding that even the specification’s “statement that the invention is ‘uniquely characterized’ by the expression of exogenous DNA sequences does not impel” the conclusion that an independent claim required use of such DNA sequences where other independent claims expressly required use of them).

Nor does the prosecution history lend support to Defendants’ position. As Shire explained in its opening brief, the prosecution history confirms that the applicants intended “pharmaceutical composition” to have its ordinary meaning. Pls. Br. at 7. Defendants ignore the



applicants' statements about "pharmaceutical composition," *id.* at 7-8 (citing JA 241-43), and mistakenly seize on the applicants' statement about their discovery that selected hydrates are "particularly effective" in binding phosphate. Defs. Br. at 15-16 (quoting JA 238). To be sure, this statement demonstrates that the inventions concern certain crystalline forms of lanthanum carbonate found to be "particularly effective" (*see also infra* Part II.B), and the claim requires at least one of those crystalline forms to be present in a composition. But this statement does not purport to impose any limitation on *how much* of those crystalline forms must be present in a composition.<sup>2</sup>

Claim 1 includes no limitation that "the amount of  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  present in the composition" where  $x$  is between 3 and 6 must itself be effective to treat hyperphosphatemia. Thus, to the extent the claim term "pharmaceutical composition for the treatment of hyperphosphatemia" requires construction, it should be construed as a "therapeutic mixture (*i.e.*, one which is sterile, reasonably safe and non-toxic) suitable for administration into the gastrointestinal tract for the treatment of hyperphosphatemia."

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<sup>2</sup> In addition, Claim 1 is written in "open" form, *see* Pls. Br. at 7, making clear that the beneficial lanthanum carbonate hydrates specified in the claim might be combined with other medicaments in formulating a therapeutic composition.

**B. “Lanthanum Carbonate Of The Formula  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  Wherein x Has A Value From” (Claims 1, 7)**

<b>Term To Be Construed</b>	<b>Shire’s Proposal</b>	<b>Defendants’ Proposal</b>
<b>lanthanum carbonate of the formula <math>\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}</math> wherein x has a value from [3 to 6 (claim 1)], [3.5 to 5 (claim 2)], [3.8 to 4.5 (claim 3)]</b>	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate, wherein x has a value from	the lanthanum carbonate present in the composition has an average water content equivalent to a water to $\text{La}_2(\text{CO}_3)_3$ mole ratio from

The parties disagree as to the meaning of the formula “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  wherein x has a value from 3 to 6.”<sup>3</sup> Shire urges that the formula refers to specific crystalline forms of lanthanum carbonate, which have particular ratios of water to lanthanum carbonate in the crystal lattice. In the art, these crystalline forms are referred to as “hydrates.” *See, e.g.*, JA 6018-19; Myerson Decl. ¶¶ 22,25. Defendants, in contrast, do not interpret the formula as relating to crystalline forms at all. Rather, they argue that it should be defined as the average water content across a sample, without regard to the crystalline forms present. Thus, under Defendants’ proposal, a sample containing only hydrates outside the claimed range mixed in proportions that yield an average water content between 3 and 6 – *e.g.*, a mixture of equal parts lanthanum carbonate monohydrate and lanthanum carbonate octahydrate, having an average water content of 4.5 – would be within the claims.

This is the central distinction between the parties’ positions. Under Shire’s proposal, a composition must contain one of these recited crystalline forms to be within the claims, although it can also contain other hydrates (because the claim is an “open” claim, *see supra* n.2). Under Defendants’ proposal, all that matters is the average water content of the entire sample. Thus,

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<sup>3</sup> For convenience, the numerical range stated in Claims 1 and 7 ( $x = 3$  to 6) is used here. Dependent claims state a narrower range:  $x = 3.5$  to 5 in Claims 2 and 8; and  $x = 3.8$  to 4.5 in Claims 3 and 9. *See* JA 8.

even a sample containing only material described in the '976 Patent as distinct from and inferior to the hydrates of the invention – *e.g.*, the octahydrate and monohydrate forms, *see* JA 6-7 ('976 Patent, Col. 1:48-51, 3:35-42) – would fall within the claims under Defendants' proposal so long as the sample's average water content was between 3 and 6.

Defendants' proposal is wholly at odds with any reasonable understanding of the claim language. Indeed, Defendants' own experts admit that it does not comport with the teachings of the '976 Patent, the description of the invention in the specification and prosecution history, and the way a person of ordinary skill would understand the claim language. *See* JA 8051-52, 8144-45 (Brittain Dep. Tr. at 52:19-53:1, 145:3-146:13).

**1. Defendants' Proposed Construction Is Inconsistent With The Plain Meaning.**

Although claim construction “begin[s] . . . with the plain language of the claim,” *Scantibodies Lab., Inc. v. Immunotopics, Inc.*, No. 2009-1481, 2010 WL 1804137, at \*2 (Fed. Cir. May 6, 2010) (unpublished) (citing *Phillips*, 415 F.3d at 1312), Defendants fail to address the plain meaning of “La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub>·xH<sub>2</sub>O.” As Shire demonstrated in its opening brief, the ordinary and customary meaning of the formula “La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub>·xH<sub>2</sub>O” is a lanthanum carbonate hydrate having “x” water molecules as part of the crystal structure per unit of lanthanum carbonate, *i.e.*, a crystalline form of lanthanum carbonate having x “waters of hydration” or “waters of crystallization.” *See* Pls. Br. at 11-12; Myerson Decl. ¶¶ 26-27, 41-42, 50.

This ordinary meaning is reinforced by the testimony of Defendants' own experts, who conceded that the ordinary meaning of “La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub>·xH<sub>2</sub>O, wherein x has a value from 3 to 6” to a person of ordinary skill in the art refers to particular species (*i.e.*, forms) of lanthanum carbonate. They agreed that “La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub>·xH<sub>2</sub>O” refers to a particular lanthanum carbonate *hydrate*, that is, a crystalline form having x moles of H<sub>2</sub>O per mole of La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub> in its crystal lattice. *See* Defs. Br.

at 3 (“These compounds are referred to as lanthanum carbonate *hydrates* and are represented by the chemical formula  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ ”) (emphasis in original). For example, Dr. Brittain admitted that “ $\text{La}_2(\text{CO}_3)_3 \cdot 8\text{H}_2\text{O}$ ” refers to lanthanum carbonate octahydrate, JA 8054-55 (Brittain Dep. Tr. at 55:18-56:1); used “ $\text{La}_2(\text{CO}_3)_3 \cdot 3\text{H}_2\text{O}$ ” in his declaration to refer to lanthanum carbonate trihydrate, Brittain Decl. ¶ 30, *see also* JA8044-45 (Brittain Dep. Tr. at 45:22-46:5); used “ $\text{La}_2(\text{CO}_3)_3 \cdot 6\text{H}_2\text{O}$ ” to refer to lanthanum carbonate hexahydrate, JA8045-46 (Brittain Dep. Tr. at 46:25-47:4); Brittain Decl. ¶ 30; and acknowledged that this formula is standard nomenclature for hydrates, JA 8047 (Brittain Dep. Tr. at 48:8-15). Indeed, Dr. Brittain refers in his declaration to “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  where x is less than 8” as “lower *hydrates* of lanthanum carbonate.” Brittain Decl. ¶ 27. Dr. Dunbar similarly agreed that “ $\text{La}_2(\text{CO}_3)_3 \cdot 3\text{H}_2\text{O}$ ” refers to lanthanum carbonate trihydrate, JA 8272 (Dunbar Dep. Tr. at 70:15-24), that “ $\text{La}_2(\text{CO}_3)_3 \cdot \text{H}_2\text{O}$ ” refers to lanthanum carbonate monohydrate, JA 8279 (*id.* at 77:8-10); and more generally that  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  refers to copper sulfate *pentahydrate* and  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$  refers to calcium sulfate *dihydrate*. JA 8259 (Dunbar Dep. at 57:12-22). This, of course, is consistent with the specification, which refers to the invention as “selected lanthanum carbonate hydrates.” JA 1 (’976 Patent, Abstract); *see also* JA 6 (*id.*, Col. 2:61-63 (“certain lanthanum carbonate hydrates”)).

Moreover, “hydrate,” by its ordinary meaning, refers to a crystalline form having water bound as part of its crystal lattice. *See, e.g.*, Myerson Decl. ¶ 25. Consistent with this ordinary meaning, Defendants’ expert, Dr. Brittain, uses “ $\text{La}_2(\text{CO}_3)_3 \cdot 8\text{H}_2\text{O}$ ” to refer to the lanthanum carbonate octahydrate species, *see* Brittain Decl. ¶ 25, which he admitted is a specific crystalline form of lanthanum carbonate containing eight moles of water as part of its crystal structure per mole of lanthanum carbonate, *see* JA 8053-55 (Brittain Dep. Tr. at 54:19-56:1). *Accord* JA 8463 (Myerson Dep. Tr. at 43:7-12). Dr. Brittain also cited in his declaration “a standard reference

text regarding inorganic structures” available before the filing of the ’976 Patent, which similarly illustrates the ordinary meaning of “hydrate.” JA 8093-94 (Brittain Dep.Tr. at 94:16-95:12 (citing A.F. WELLS, STRUCTURAL INORGANIC CHEMISTRY (5th ed. 1984))). This reference explains that “[t]he term hydrate should be used only for *crystalline* compounds containing H<sub>2</sub>O molecules . . . .” JA 6018-19; JA 8093-94 (Brittain Dep. at 94:16-95:12); *see also* JA 8093-96 (Brittain Dep. Tr. at 93:15-96:22).<sup>4</sup>

In addition, Defendants’ experts admitted in deposition that the formula “La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub>·xH<sub>2</sub>O” used in the claims would *not* be understood to refer to an average water content of a mixture of different crystalline forms. As Defendants’ expert, Dr. Dunbar, agreed, “to a person of ordinary skill, a 50/50 blend of lanthanum carbonate monohydrate and lanthanum carbonate octahydrate would not be described as La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub>·4.5H<sub>2</sub>O” although it would have an average water content of 4.5. JA 8279-80 (Dunbar Dep. Tr. at 77:17-78:25). Dr. Dunbar explained that a physical mixture of the compounds would still have “the individual characteristics of these two compounds,” and “hence different phosphate binding capabilities” than a form of lanthanum carbonate with 4.5 waters of hydration. *Id.* Dr. Brittain similarly admitted that the ’976 Patent “would *not* be understood to refer to” compositions “containing a mixture of different stoichiometric lanthanum carbonate hydrates.” JA 8050-51, 8144-45 (Brittain Dep. Tr. at 51:13-53:1, 152:2-153:3).<sup>5</sup>

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<sup>4</sup> In scientific papers, Dr. Brittain has similarly defined hydrates as “crystalline solid adducts containing solvent molecules *within the crystal structure*,” in which the solvent is water. JA 6061 (S.R. Vippagunta, H.G. Brittain & D.J.W. Grant, *Crystalline Solids*, 48 ADV. DRUG. DEL. REV. 3, 4 (2001) (emphasis added)).

<sup>5</sup> Defendants’ counsel plainly recognized the devastating nature of this concession; he repeatedly tried to obstruct questioning on this subject. *See* JA 8139-43 (Brittain Dep. Tr. at 140:11-144:8).

These admissions are fatal to Defendants' proposed construction. The Federal Circuit has made clear that claims should be construed according to how skilled artisans would understand the claim language. *See, e.g., Phillips*, 415 F.3d at 1312-13. Defendants' own experts admit, consistent with the opinions offered by Dr. Myerson, that skilled artisans would not understand the claim as Defendants propose to construe it. Rather, the recited formula would be understood to refer to particular species of lanthanum carbonate.

Thus, there is no genuine dispute over the ordinary and customary meaning of the claim term " $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ , wherein x has a value from 3 to 6." That term is standard nomenclature to refer to specific crystalline forms of lanthanum carbonate having a ratio of x moles of water to a mole of lanthanum carbonate in the crystal lattice (*i.e.*, lanthanum carbonate hydrates having "x" waters of hydration). And that is the controlling meaning for purposes of claim construction.

## **2. The Intrinsic Evidence Does Not Show That The Inventors Intended To Depart From The Ordinary And Customary Meaning.**

Defendants seem to argue that the specification or prosecution history alters the plain meaning of " $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ , wherein x has a value from 3 to 6," providing it a special definition in the '976 Patent. They are incorrect. The Federal Circuit has explained that "[t]he specification may impart a definition that differs from a term's ordinary meaning only when it demonstrates 'an intent to deviate from' that meaning," *University of Pittsburgh v. Hedrick*, 573 F.3d 1290, 1296 (Fed. Cir. 2009) (citation omitted), and that "[t]he plain and ordinary meaning of claim language controls, unless that meaning renders the claim unclear or is overcome by a special definition that appears in the intrinsic record with reasonable clarity and precision," *DSW*, 537 F.3d at 1347 (internal quotation marks omitted). Defendants cannot meet the burden to show that the specification or prosecution history alters the plain meaning of the term. Far from showing with the requisite "clarity and precision" that the inventors applied a special

definition to the chemical formula, the intrinsic evidence shows that the inventors used the term “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ , wherein x has a value from 3 to 6” according to its plain meaning. *See* Pls. Br. at 13-16.

**a) Defendants’ Proposed Departure From The Plain Meaning Rests On Faulty Scientific Premises And A Misreading Of The Specification.**

Defendants argue that the specification alters the ordinary meaning of “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ , wherein x has a value from 3 to 6,” based on a misreading of the specification. Defendants not only ignore much of the intrinsic evidence, they rely principally on three arguments resting on scientific errors.

*First*, Defendants present a false dichotomy. They argue that if the chemical formula does not refer to a single *molecule* of lanthanum carbonate having the recited amount of water, it must refer to average water content across a whole composition. Defs. Br. at 7. The solids at issue here, however, are crystals, and the relevant unit for analysis of a crystal is not a molecule but a structure called a “unit cell.” JA 8060-61 (Brittain Dep. Tr. at 61:9-62:11 (unit cell is the “fundamental building block that is repeated through all three dimensions . . . to create the crystal”)); *see also* Myerson Decl. ¶ 21. The unit cell of lanthanum carbonate octahydrate, for example, contains four formula units of lanthanum carbonate and thirty-two water molecules (thus having a ratio of eight water molecules to one unit of lanthanum carbonate). JA 8060-62 (Brittain Dep. Tr. at 61:9-63:14); JA 6089-97. Even lanthanum carbonate octahydrate will have no definable “molecule” of lanthanum carbonate containing eight water molecules, yet the experts all agree that “octahydrate” refers to a well-defined crystal structure and not an average water content across a composition. JA 8057-69 (Brittain Dep. Tr. at 58:13-70:1); JA 8238, 8240-41 (Dunbar Dep. Tr. at 36:4-12, 38:1-39:5); JA8581-82 (Myerson Dep. Tr. at 161:18-162-3); *see also* JA 6092-97.

*Second*, Defendants make the scientifically erroneous argument that the specification's disclosure of non-integer hydrates compels the conclusion that the chemical formula refers to a composition's "average water content" rather than a crystalline form. Defs. Br. at 7-8, 11. Defendants disregard that non-integer hydrates – crystalline forms having a non-integer number of water molecules as part of their crystal structure per unit of the solvate – are well-known. Defendants' own expert, Dr. Dunbar, admitted in deposition that "in the field of inorganic chemistry it is not uncommon to see non-integer waters of hydration." JA 8284-85 (Dunbar Dep. Tr. at 82:9-83:23). Dr. Myerson explained that well-defined hydrates often have a non-integer value of "x." Myerson Decl. ¶¶ 27-29, 51. The Wells book that Dr. Brittain cites and considers a "standard reference" provides many examples of non-integer hydrates. JA 6022-6040; *see also* JA 8103-17 (Brittain Dep. Tr. at 104:23-118:14). Indeed, the Yanagahira article cited in the prosecution history, in explaining that lanthanum carbonate hydrates having different waters of hydration can be distinguished using infrared spectroscopy, references a non-integer lanthanum carbonate hydrate: "[i]t has been reported that the number of molecules of water associated with lanthanum carbonate varied from 8 to 5.5." JA 203 (emphasis added). Thus, the specification's disclosure of decimals is consistent with the formula referring to particular crystalline forms of lanthanum carbonate having the specified number of water molecules bound as part of the crystal lattice per unit lanthanum carbonate. It in no way supports construing the term as anything other than its ordinary meaning.

The written description further demonstrates that the non-integers are consistent with the ordinary meaning of the formula, because it makes clear that the non-integer waters of hydration derive from experiments in which crystalline water was removed from higher-order lanthanum carbonate hydrates through a controlled drying process. JA 8435-36 (Myerson Dep. Tr. at 15:11-16:8); *see also* JA 8436-40 (*id.* at 16:19-20:11). The inventors conducted experiments



starting with lanthanum carbonate octahydrate, subjecting it to sufficient heat to remove water from the lattice. JA 8452 (Myerson Dep. Tr. at 32:7-8); *see also* Brittain Decl. ¶ 27. Because the water molecules contribute to the structure of the crystal, removing water molecules causes the lattice to break down in regions within the crystal; localized amorphous regions form as the structure converts to the tetrahydrate form. The partially dehydrated material remains crystalline, but instead of being a theoretical “perfect” crystal, it will contain localized regions having less order. JA 8446-47, 8449, 8453-54, 8455 (Myerson Dep. Tr. at 26:23-27:11, 29:5-13, 33:13-34:7, 35:15-18). This is akin to removing beams from a house, causing portions of the roof to collapse while the remainder of the house remains intact. In these partially dehydrated hydrates, the crystal has a non-integer number of water molecules per unit of lanthanum carbonate. Because water is removed uniformly from crystals in the small samples, each crystal will have this same ratio and the same form. JA 8444-46, 8548-49 (Myerson Dep. Tr. at 24:22-26:8; 128:18-129:25).<sup>6</sup> Thus, the relevant unit of analysis remains a single crystal and the relevant water is that within the crystal lattice, not some average water content across an entire sample.

*Third*, Defendants erroneously assert that the measurement techniques disclosed in the specification can provide information only about average water content, and not any identification of species. Defs. Br. at 8-11. In fact, the techniques disclosed are those that

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<sup>6</sup> A skilled artisan would also understand certain of the non-integer experimental values reported in the specification to reflect experimental error in the measurement of the tetrahydrate form, as well as the presence of vacancies and defects ordinarily present in real-world (as opposed to theoretical) crystals. JA 8441-42 (Myerson Dep. Tr. at 21:3-22:22); *see also* JA 8446-47 (*id.* at 26:9-27:11) (referring to the 3.8 and 4.4 hydrates as tetrahydrate that was either slightly over-dried or under-dried); JA 8470-71, 8525 (*id.* at 50:15-51:16, 105:4-18). Figure 4 of the '976 Patent shows, as reported in earlier literature, that a distinct lanthanum carbonate tetrahydrate structure exists when four waters of crystallization are removed from the octahydrate. JA 6084-88 (“Oda” reference); JA 8444-45 (Myerson Dep. Tr. at 24:17-25:8).

skilled artisans would use to characterize the crystalline forms of a material. JA 8582-85 (Myerson Dep. Tr. at 162:20-165:2).

To argue otherwise, Defendants ignore the specification's disclosure of x-ray powder diffraction (XRPD) testing. XRPD is routinely used in the pharmaceutical industry for the very purpose of characterizing crystalline forms. Myerson Decl. ¶ 32. It provides information about crystal structure and *not* average water content. Brittain Decl. ¶ 60 ("XRPD analysis could not be used to determine an average value of 'x.'"). Two of the four figures in the specification (Figures 3 and 4) disclose diffraction patterns from XRPD providing "fingerprints" for the octahydrate and tetrahydrate crystal structures. JA 4-5, JA 6 ('976 Patent, Figs. 3-4, Col. 2:30-35, 2:40-41); Myerson Decl. ¶ 31.

Further, Defendants make the faulty assertion that "thermal methods such as TGA can only provide information regarding an average value for 'x,'" Brittain Decl. ¶ 49, which their own expert contradicts. Dr. Dunbar explained, consistent with Dr. Myerson and much literature, that thermogravimetric analysis (TGA) can be used to analyze the formation of new hydrates as water is removed from a sample. JA 8514, 8516-17, 8548-49 (Myerson Dep. Tr. at 94:13-21, 96:24-25, 97:1-19, 128:14, 129:20); JA 8255, 8256-61, 8262-63 (Dunbar Dep. Tr. at 53:18-23, 54:19-59:21, 60:12-61:25); *see also* MICHAEL E. BROWN, INTRODUCTION TO THERMAL ANALYSIS (1988), Dunbar Decl. Ex. 7 at 17-21. Removing water from lanthanum carbonate octahydrate and analyzing the lower order hydrates is precisely what the inventors were doing in the testing described in the '976 Patent, as even Dr. Brittain acknowledged. *See* JA 8126-27 (Brittain Dep. Tr. at 127:25-128:13) (experiment disclosed in Table 1 aimed to "determine . . . rates of phosphate removal . . . by lanthanum carbonate *species* that had been prepared by *different degrees of drying*" octahydrate); *see also* JA 6 ('976 Patent, Col. 2:36-53).

In addition, Defendants draw unsupportable inferences from the data reported in a table in Column 2 of the Patent. Defendants argue that skilled artisans “would understand from these calculations of ‘x’, which are based on water loss upon drying the samples over time, that ‘x’ is an average value that can *only* reflect the total water content of the sample that was being tested.” Defs. Br. at 10 (emphasis added); *see also id.* at 6. The table does not, however, purport to *define*  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ , and certainly not with the clarity needed to displace the ordinary and customary meaning of the term. Thus, it cannot justify departure from the customary meaning of  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ . In any event, the calculations are fully consistent with the ordinary meaning of the formula, given the special conditions described by the specification for this testing, which Defendants ignore. The table illustrates a special case where the average water content is indicative of the crystalline species present because the sample is homogenous and any extra-crystalline water (*i.e.*, moisture loosely bonded to the surface of a crystal rather than within the crystal lattice) has been removed through a controlled drying process.

The specification teaches that special conditions were used to assure that the samples tested were homogenous. *See, e.g.*, JA 7 (Example 1, Col. 4:10-15). The inventors characterized their starting material using four separate tests, determining it was lanthanum carbonate octahydrate that had a specified amount of surface water. JA 6 ('976 Patent, Col 2:38-42). They then heated small samples under controlled conditions to remove water homogeneously, and measured the weight loss. Skilled artisans would recognize that surface water will be removed first, that the remaining weight loss will be attributable (within experimental error) to water removed from the crystal lattice of what initially was lanthanum carbonate octahydrate, and that the removal of water will occur uniformly in the crystals making up the sample. JA 8548-49 (Myerson Dep. Tr. at 128:14-129:25); JA 8545-46 (*id.* at 125:23-126:22). Under these special conditions of drying a homogenous sample, using loss of drying to determine the value x

indicates the crystalline form present (*i.e.*, the number of moles of water per mole of lanthanum carbonate in the resultant crystalline material) as well as the average water content.

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Yet Defendants’ proposed construction does not limit a composition to these special conditions where an average is indicative of the species present.

In addition to mischaracterizing underlying scientific principles, Defendants’ ignore the overwhelming intrinsic evidence that the inventors intended the formula to carry its ordinary and customary meaning. Claim 5 indicates that the claimed formula is “lanthanum carbonate with 3 to 6 molecules of *water of crystallization*.” *See* Pls. Br. at 13. The specification consistently states that the invention concerns the discovery that particular “forms” of lanthanum carbonate (“selected lanthanum carbonate hydrates” having 3-6 “waters of crystallisation”) have advantageous properties, and provides XRPD data displaying differences in the crystalline forms. JA 1, JA 6 (’976 Patent, Abstract, Col. 2:9-12); *see also* JA 6 (’976 Patent, Col 2:61-64); JA 8462-63, 8472, 8500-02 (Myerson Dep. Tr. at 42:17-43:3; 52:10-15; 80:23-82:17). Skilled artisans would further recognize that the ability of “selected” hydrates to bind phosphate “appreciably quicker” relates to differences in their crystal structure. JA 7 (’976 Patent, Col. 3:20-43). *See* Myerson Decl. ¶ 23 (different crystal structures exhibit different physical properties from each other); *accord* JA 8294-95 (Dunbar Dep. Tr. at 92:11-93:4); JA 8124 Brittain Dep. Tr. at 125:15-24 (“the crystal structure determines everything about an inorganic compound”).

Accordingly, a skilled artisan would read the specification to confirm that “La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub>·xH<sub>2</sub>O” means what it says—as representing “selected hydrates” of lanthanum carbonate, not an average of the water in an undifferentiated mass of bulk drug substance,

whether or not that water was bound to the lanthanum carbonate and whether or not that substance is homogenous or a mixture.

**b) Defendants' Proposed Construction Is Contradicted By The Prosecution History.**

The prosecution history overwhelmingly supports the conclusion that the formula was used according to its ordinary and customary meaning in the '976 Patent. As Defendants' expert, Dr. Brittain, recognized, "the Applicants described the invention" as "the unexpected discovery that *lanthanum carbonates with waters of crystallization or hydration between 3 and 6 moles of water per mole of lanthanum carbonate* are particularly effective in absorbing phosphate both *in vivo* and *in vitro*." Brittain Decl. ¶ 76 (quoting [JA 238] (emphasis added)). This choice of words is significant. "Waters of hydration," like "waters of crystallization," has a customary meaning consistent with Shire's proposed construction and contrary to Defendants'. JA 8044, 8068-69, 8080 (Brittain Dep. Tr. at 45:4-16, 69:20-70:1, 81:11-23). As explained in Shire's opening brief, and further supported by Defendants' experts, these terms refer to water bound as part of a crystal lattice. Pls. Br. at 10-11, 13; JA 8037-39 (Brittain Dep. Tr. at 38:4-40:5); *see also* Myerson Decl. ¶ 26. Defendants simply ignore these consistent statements in the prosecution history defining the claimed invention as particular lanthanum carbonate hydrates having "waters of crystallization" or "waters of hydration" of 3-6, *see* Pls. Br. at 13-16; Myerson Decl. ¶¶ 46-49.

Defendants instead rely upon a single statement from the British patent application preceding the application filed in the United States to argue that  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  cannot carry its ordinary meaning because lanthanum carbonate tetrahydrate purportedly is amorphous. Defs. Br. at 13-14. This argument lacks any merit, and illustrates the danger of reliance on isolated pieces of the prosecution history.

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Dr. Brittain admitted that he was unaware of any other document or reference reporting amorphous lanthanum carbonate hydrates. JA 8081-82 (Brittain Dep. Tr. at 82:11-83:11). The British document refers to tetrahydrate as having a specific “form,” JA 116, and

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When the applicants filed their application in the United States (which matured into the '976 Patent), they provided x-ray diffraction patterns for both the tetrahydrate and octahydrate forms and, notably, when they did so, they no longer stated that the tetrahydrate was amorphous. *See* JA 0093-0113; *see also* JA 8462-64 (Myerson Dep. Tr. at 42:17-44:4). They removed this statement for good reason: The patterns provided demonstrate that both forms are crystalline. JA 6 ('976 Patent, Col. 2:30-35, Figs. 3 and 4); Myerson Decl. ¶ 31; JA 8559-60 (Myerson Dep. Tr. at 139:14-140:2).

As Defendants' expert, Dr. Dunbar, explained in her declaration, a solid is either crystalline or amorphous; the categories are mutually exclusive. *See* Dunbar Decl. ¶ 18. An amorphous solid lacks any long-range order, while a substance having some long-range order, even if it is not perfectly ordered, is crystalline. *See id.* ¶¶ 19-20. When characterized using x-ray powder diffraction, an amorphous solid will display a “halo,” not peaks. *See, e.g.,* JA 8025 (Brittain Dep. Tr. at 26:2-16) (“The diffraction pattern of an amorphous material will not exhibit sharp peaks and in fact will consist of effectively simply broad diffraction. No sharp peaks and it will consist of this very broad smear . . . that people refer to as the amorphous halo.”). Figure 3

of the '976 Patent, however, which shows results of XRPD on the tetrahydrate form, shows peaks, illustrating that the tetrahydrate is crystalline. JA 8539-42 (Myerson Dep. Tr. at 119:12-122:2). Its broader peaks may reflect amorphous regions within the crystal, but the material is crystalline nonetheless. Indeed, neither of Defendants' experts has suggested that Figure 3 exhibited the "amorphous halo" referred to by Dr. Brittain.

The inclusion of XRPD data in the patent application filed in the United States (which issued as the '976 Patent), and the repeated references to crystalline hydrates – *see, e.g.*, JA 1 ('976 Patent, Abstract); JA 6 ('976 Patent, Col. 1:48-52, Col. 2:61-64) – would make it plain to person of ordinary skill in the art that the patented invention is directed to specific crystalline forms of lanthanum carbonate, and not purely amorphous material. Indeed, the claim language " $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ , wherein x has a value from 3 to 6" is nomenclature used to identify crystalline material, not amorphous material. *See supra* Part II.B.1.

Thus, rather than supporting Defendants' proposed construction, their overreading of an isolated statement in British application illustrates the pitfalls of relying on prosecution history divorced from context. *See Phillips*, 415 F.3d at 1317 (prosecution history "often lacks the clarity of the specification and is thus less useful for claim construction purposes").

Not only does the '976 Patent illustrate that lanthanum carbonate tetrahydrate is crystalline, the Oda reference cited in the prosecution history teaches that lanthanum carbonate trihydrate and pentahydrate are also crystalline. JA 6086. Defendants' experts failed to consider this reference, despite its citation on the face of the '976 Patent and the fact that its very title, "Studies on *Crystal Waters* of Lanthanum Carbonates," discloses its relevance to the issues here. *See* JA 6084-88 (full article); JA 1 (citation in '976 Patent); JA 197 (abstract in file history). Defendants thus mistakenly assert that the lower order hydrates of lanthanum carbonate were unknown, when Oda discloses precisely such hydrates. It discloses lanthanum carbonate

hydrates with 1, 3 and 5 molecules of water per formula unit of lanthanum carbonate and x-ray diffraction patterns identifying them. JA 6086; *see also* JA 197 (Oda abstract noting that “[t]he thermal behaviors of  $\text{La}_2(\text{CO}_3)_3 \cdot n\text{H}_2\text{O}$  crystals ( $n = 1, 3, 5, 8$ ) were studied by DTA, x-ray powder diffractometry, and IR spectroscopy.”). The Oda article, available to a skilled artisan as of the time of the ’976 Patent, clearly indicates that lanthanum carbonate trihydrate, pentahydrate and octahydrate are distinct crystalline structures, JA 6086; JA 8452-53 (Myerson Dep. Tr. at 32:21-33:7), and that the octahydrate form can be dried to a tetrahydrate form, REDACTED

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*see also* JA 8444-45, 8509, 8511-12

(Myerson Dep. Tr. at 24:17-25:21, 89:5-14, 91:19-92:13).

Thus, far from demonstrating with the requisite clarity that the inventors intended to alter the plain meaning of “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ , wherein  $x$  has a value from 3 to 6,” the prosecution history – especially its consistent description of the inventions as “lanthanum carbonates with waters of crystallization or hydration between 3 and 6 moles of water per mole of lanthanum carbonate,” *see, e.g.*, JA 238 – shows that the inventors used the term according to its ordinary and customary meaning.

### **3. Defendants’ Reliance On Extrinsic Evidence To Alter the Plain Meaning Of The Claim Term Is Inappropriate.**

To support their proposed construction, Defendants cite isolated statements from the

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Even were the Defendants faithful to Dr. Murrer’s testimony, which they are not, this extrinsic evidence would be of little import under longstanding authority. The Federal Circuit “has often repeated that inventor testimony is of little probative value for purposes of claim construction,” *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1370 n.5 (Fed. Cir. 2003), and “cannot be relied on to change the meaning of the claims” as Defendants



attempt to use it for here, *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 983 (Fed. Cir. 1995) (*en banc*); *see also Howmedica Osteonics Corp. v. Wright Med. Tech., Inc.*, 540 F.3d 1337, 1346-47 (Fed. Cir. 2008) (*quoting Markman*, 52 F.3d at 985). Indeed,

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In any event, Dr. Murrer's testimony fails to support Defendants' position.<sup>7</sup> Only by carefully culling his testimony and removing its context can Defendants assert otherwise. Significantly,

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<sup>7</sup> If the Court is inclined to consider inventor testimony, it should also consider the testimony of Dr. Peter Davies, an inventor of the '428 patent, which uses the same chemical formula. He testified that the formula in Claim 1 of the '976 Patent "is standard chemical notation for waters of hydration," JA 6109 (Davies Dep. Tr. at 49:21-25), and that "waters of hydration" means "water that is associated with the crystal structure of the lanthanum carbonate, so we are talking about waters that are bound in some way to the crystal of the lanthanum carbonate." JA 6105 (Davies Dep. Tr. at 15:6-16). Dr. Davies further explained that the "crystal form" of lanthanum carbonate can be determined by XRPD and TGA, two techniques disclosed in the '976 Patent. JA 6106-07 (Davies Dep. Tr. at 26:4-27:10).

<sup>8</sup> Defendants resort to relying on extrinsic evidence that by its own terms says nothing about how a person of ordinary skill would understand the claim language of the '976 Patent: an  
(continued...)

Finally, Defendants mistakenly rely on statements made in an application for a Patent Term Extension filed by Shire years after the issuance of the '976 Patent. Defs. Br. at 12. The Patent Term Extension papers are extrinsic evidence, not part of the prosecution history. *See Abbott Labs. v. Dey*, 110 F. Supp. 2d 667, 673 (N.D. Ill. 2000) (treating Patent Term Extension papers as extrinsic evidence). In contrast to the prosecution history, which “informs the meaning of claim language by demonstrating how the inventor and the Patent Office understood the invention at the relevant time period,” *Phillips*, 415 F.3d at 1317, the Patent Term Extension submission was not part of any such negotiation about the scope of the claims. Rather, it was filed in December 2004 – five years after the patent had issued. *See* JA 271.

In any event, the Patent Term Extension application fails to support Defendants’ proposed construction. If “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ ” were actually understood to refer to the “average water content” of the lanthanum carbonate in a composition as Defendants contend, it would have made little sense for Shire to specify that in Fosrenol “x is *an average* of 4.5,” as opposed to just “x = 4.5.” JA 271 (emphasis added).

\* \* \*

For the reasons set forth above and in Shire’s opening papers, the term “lanthanum carbonate of the formula  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  wherein x has a value from” should be construed according to its ordinary and customary meaning, as “a crystalline form of lanthanum carbonate

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REDACTED It is well established that extrinsic evidence cannot be used to vary or contradict meaning apparent from intrinsic evidence. *Vitronics Corp. v. Conception, Inc.*, 90 F.3d 1576, 1585 (Fed. Cir. 1996).

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containing x moles of water as part of its crystal structure per mole of lanthanum carbonate, wherein x has a value from.”

**C. “Unit Dosage Form To Provide From 0.1 To 20g/day” (Claim 4)**

<b>Term To Be Construed</b>	<b>Shire’s Proposal</b>	<b>Defendants’ Proposal</b>
<b>unit dosage form to provide from 0.1 to 20g/day</b>	a solid or liquid form used to administer a dose of between 0.1 and 20g/day of elemental lanthanum	one or more unit dosage forms to provide a total daily dose of from 0.1 to 20 g/day of $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$

The parties’ dispute about this claim term centers on whether dosing is stated in terms of elemental lanthanum (as Shire proposes) or the lanthanum carbonate hydrate used (as Defendants propose). The specification clearly resolves this dispute: It demonstrates that the ’976 Patent described dosing of lanthanum carbonate hydrates based on the amount of elemental lanthanum, Pls. Br. at 17-19; Scheel Decl. ¶¶ 27-33, consistent with how prior art phosphate binders were dosed and how lanthanum carbonate phosphate binders are dosed, Pls. Br. 18; Scheel Decl. ¶¶ 31-32.

A skilled artisan would understand the dosing stated in Claim 4 to refer to a daily dose of elemental lanthanum because it is the lanthanum—not the entire lanthanum carbonate hydrate—that binds with the phosphate; the lanthanum does so after the carbonate and water molecules disassociate in a patient’s gastrointestinal tract. *See* Scheel Decl. ¶ 30; JA 8345-47 (Scheel Dep. Tr. at 39:16-41:3). Dr. Scheel’s opinion stands undisputed. Defendants only argument is based on an opinion offered by their expert, Dr. Brittain, who is not a medical doctor, let alone a nephrologist, has never treated hyperphosphatemia, has no experience with dosing regimes for hyperphosphatemia treatments, and did not even consider how prior art compounds were dosed to treat hyperphosphatemia. JA 8012-13, 8131-34 (Brittain Dep. Tr. at 13:17-14:9, 132:14-135:7).

Defendants' assertion that the intrinsic evidence does not address the use of elemental lanthanum is clearly mistaken. Defs. Br. at 17-18. Their expert, Dr. Brittain, acknowledged that a skilled artisan would understand that it is *elemental lanthanum* that binds with phosphate and that in the phosphate binding experiment described in the specification, amounts of different lanthanum carbonate hydrates were adjusted to hold constant the proportion of *elemental lanthanum* to phosphate and thus dosed in terms of elemental lanthanum. See JA 8128-31 (Brittain Dep. Tr. at 129:13-132:13); see also Pls. Br. at 17-18 (citing JA 6-7 ('976 Patent, Col. 2:61-3:42)). These phosphate binding experiments were designed to simulate the conditions under which a phosphate binder would work in a patient and thus provide strong evidence that dosing is stated in terms of elemental lanthanum. JA 8383-84 (Scheel Dep. Tr. at 77:6-78:18); JA 8128 (Brittain Dep. at 129:5-11); see also JA 7 ('976 Patent, Col. 3:1-8) (experiments carried out at pH of 3); JA 240 (11/19/98 Amendment and Remarks) (noting that the *in vitro* experiment "a solution at pH 3, close to the pH level found in the digestive tract was used."). The mere fact that the specification does not use the word "elemental" (Defs. Br. at 18; Brittain Decl. ¶ 69)) is irrelevant to how a skilled artisan would understand the units used for dosing. Given the intrinsic evidence, the unchallenged testimony of Shire's expert nephrologist and the admissions of Defendants' expert, it cannot be disputed that a person of ordinary skill in the art would understand the '976 Patent's reference to dosing to be in terms of elemental lanthanum.

By contrast, the intrinsic evidence cited by Defendants does not show how lanthanum carbonate is dosed. Defendants' brief conspicuously ignores the phosphate binding experiment described in the specification, instead of relying on two isolated statements from the specification. Defs. Br. at 17-18. The first, Column 1, lines 64-67 (JA 6), refers to an effective dose of lanthanum carbonate but does not explain how dosing is stated and thus is inapposite to construing Claim 4. The other, Column 5, lines 30-37 (JA 8), concerns an experiment

demonstrating that lanthanum is not absorbed by patients but rather is fully excreted. This passage actually supports Shire's position. The description makes clear that "lanthanum phosphate" is "formed after binding to phosphate in the gut," indicating that (in accordance with Shire's construction) it is elemental lanthanum, not lanthanum carbonate, that is the relevant unit for purposes of determining the proper dose for treating a patient, because it is the lanthanum that actually binds with the phosphate. *Id.*

Moreover, extrinsic evidence further supports Shire's position and contradicts Defendants'. Defendants disregard that the standard practice in the field has been to dose lanthanum carbonate hydrates in terms of the amount of elemental lanthanum. Doses of Shire's Fosrenol® are stated this way. *See* JA 6133 (Fosrenol prescribing information)

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**D. "Effective To Treat Said Hyperphosphatemia" (Claim 7)**

<b>Term To Be Construed</b>	<b>Shire's Proposal</b>	<b>Defendants' Proposal</b>
<b>effective to treat said hyperphosphatemia</b>	capable, without toxic effects, of maintaining the serum phosphate level of a subject at a substantially constant level or reducing the serum phosphate level in a subject who has an excess level of serum phosphate	wherein the amount of $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ present in the composition is effective to treat hyperphosphatemia

Here again, Defendants' proposed construction would rewrite the claim by inserting an extraneous amount limitation, "wherein the amount of  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  present in the composition." Defendants' leave the very claim language purportedly being construed unchanged in their proposed construction. Moreover, Claim 7 *already* requires the use of an amount of lanthanum carbonate with between 3 and 6 moles of water per mole of lanthanum

carbonate effective to treat hyperphosphatemia; but it does so in language separate from that being construed. *See supra* Part II.A. Thus, Defendants’ proposed construction simply adds redundancy to the claim and transparently attempts to add an extraneous limitation.

Shire’s proposed construction clarifies what effective to treat hyperphosphatemia means based on the specification as it would be understood by skilled artisans. Pls. Br. at 19-20; JA 7-8 (’976 Patent, Col. 3:47-49, 3:52-53, 5:30-37); *see also* Scheel Decl. ¶¶ 34-36. As Dr. Paul Scheel, a nephrologist, explained, “each chronic kidney disease patient is different both in terms of their existing serum phosphate level and their customary diet, meaning that a given amount of lanthanum present in the composition will not be equally effective with each patient. . . . [Thus], it is more accurate to construe the term ‘effective to treat’ in this context in terms of the observed effect on the serum phosphate level of a patient.” Scheel Decl. ¶ 37. Defendants’ proposed construction, in contrast, fails to identify any metric by which to determine whether a composition is effective to treat hyperphosphatemia.

### III. THE ’465 AND ’428 PATENTS

- A. “Lanthanum Carbonate Has The Formula  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  Where x Has A Value From” (’465 Patent, Claim 3); “Lanthanum Carbonate Having The Formula  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  Wherein x Has A Value From” (’428 Patent, Claims 1 and 7)

Term To Be Construed	Shire’s Proposal	Defendants’ Proposal
<b>lanthanum carbonate has the formula <math>\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}</math> where x has a value from (’465 Patent)</b>	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate	the lanthanum carbonate present in the composition has an average water content equivalent to a water to $\text{La}_2(\text{CO}_3)_3$ mole ratio from
<b>lanthanum carbonate having the formula <math>\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}</math> wherein x has a value from (’428 Patent)</b>	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate	the lanthanum carbonate present in the composition has an average water content equivalent to a water to $\text{La}_2(\text{CO}_3)_3$ mole ratio from

The parties agree that the formula “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ ” has the same meaning in the ’465 and ’428 Patents as in the ’976 Patent. Pls. Br. at 22; Defs. Br. at 19, 23. As with the ’976 Patent, Defendants attempt to displace the ordinary meaning “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ ” with the distinct concept of average water content of a bulk drug substance. Here, too, they erroneously do so based largely on incorrect conclusions they draw from the disclosure of non-integer values of “x” (Defs. Br. at 20), and the teaching that TGA can be used to help determine “x” (*id.* at 20, 24). *See supra* Part II.B.

Defendants’ proposed construction is also inconsistent with the ’428 Patent’s disclosure that the “hydration level” of a lanthanum carbonate can be measured by XRPD. JA 0041 (’428 Patent, Col. 4:39-43). As Defendants’ own expert concedes, XRPD cannot measure average water content; rather, it measures crystal structure and thus is used to analyze crystal forms present. Brittain Decl. ¶ 60; JA 8022-23, JA 8024-25 (Brittain Dep. Tr. at 23:2-24:8, 25:2-26:16); *see also* JA 8582-85 (Myerson Dep. Tr. at 162:20-165:2). Faced with this intrinsic evidence undercutting their position, Defendants resort to asserting that a skilled artisan “would understand that XRPD is only useful to determine ‘x’ to the extent that reference patterns for various values of ‘x’ are available for comparison.” Defs. Br. at 24; Brittain Decl. ¶¶ 59-60. This is irrelevant. XRPD is a standard tool in the pharmaceutical industry to characterize a crystalline form even in the absence of an established reference pattern, JA 8582-85 (Myerson Dep. Tr. 162:20-165:2), and a patent need not be a Ph.D. thesis setting forth all known details about an invention. In any event, XRPD patterns for several lanthanum carbonate hydrates were available in the art (such as in the Oda reference, *see* JA 6084-88).

Defendants also rely heavily on a statement in the ’465 and ’428 Patents that in one preferred embodiment x may have a given “average” value. JA 0015 (’465 Patent, Col. 4:19); JA 0041 (’428 Patent, col. 4:35-40). But as Shire explained in its opening brief, by describing

“x” as having an average value in this one embodiment, the specification makes clear that “x” is not itself an average value. Pls. Br. at 23. Moreover, the specification states that “x” has an average value only in one of several preferred embodiments.

Additionally, dependent Claims 6 and 12 of the '428 Patent include *both* a limitation reciting  $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$  (incorporated from, respectively, independent Claims 1 and 7), as well as a limitation concerning “water content.” In offering the same construction for both terms, Defendants violate the presumption that different claim terms in the same claim mean different things. *See, e.g., Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 93 F.3d 1572, 1579 (Fed. Cir. 1996); *see also Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357 n.1 (Fed. Cir. 1999) (noting that it would be improper to use “two different phrases . . . to mean the same thing in the same claim”)); *Timeline, Inc. v. Proclarity Corp.*, No. C05-1013JLR, 2007 WL 321387, at \*2-3 (W.D. Wash. Jan. 31, 2007) (rejecting the argument that the term “automatically” and “without the need for human analysis” in the same claim should be construed identically - “[t]here is no apparent reason why the patentee would use [the two terms] in such close proximity in the same claim if the patentee intended the two terms to have identical meanings.”). Defendants’ proposed constructions would improperly eliminate the distinction between “water content” and “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ ,” when both terms are found in Claims 6 and 12. *See also* JA 6107-08. Moreover, to the extent the Court considers inventor testimony, Dr. Davies, an inventor on the '428 Patent, explained that waters of hydration (the value “x” in the recited formula) has a different meaning than water content: water content is the total quantity of



water present in the sample, whereas waters of hydration refers to water structurally bound in crystals. JA 6107-08 (Davies Dep. Tr. at 27:12-28:5).<sup>9</sup>

**B. “Water Content” (‘465 Patent, Claim 8), (‘428 Patent, Claims 6 and 12)<sup>10</sup>**

<b>Term To Be Construed</b>	<b>Shire’s Proposal</b>	<b>Defendants’ Proposal</b>
<b>lanthanum carbonate is hydrated having a water content of about 4 moles of water (‘465 Patent, Claim 8)</b>	lanthanum carbonate present in the tablet has a ratio of approximately 4 moles of water to one mole of lanthanum carbonate	the lanthanum carbonate present in the composition has an average water content equivalent to a water to $\text{La}_2(\text{CO}_3)_3$ mole ratio of about 4
<b>water content (‘428 Patent, Claims 6 and 12)</b>	ratio of moles of water to one mole of lanthanum carbonate	<i>Defendants have stated they cannot construe this term</i>

The parties appear to be in general agreement that the term “water content” refers to a ratio of moles of water to moles of lanthanum carbonate present in the composition. *See* Defs. Br. 21, 25. The problem is that Defendants erroneously contend that “water content” and “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ ” mean the same thing—that the lanthanum carbonate present in the composition has a certain “average water content.” This is wrong, as explained above. *See supra* Part III.A.

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<sup>9</sup> The statements in the prosecution history concerning calculation of “water content” (Defs. Br. at 24-25 (citing JA 4879-80, JA 4887-88 (11/16/07 Amendment and Remarks at 6 and Ex. 1))) are similarly inapposite. Far from equating the distinct terms “ $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ ” and “water content,” the cited document makes clear by using them both that the applicants recognized a distinction between them. These passages simply concern calculating the prescribed weight of elemental lanthanum carbonate in claimed compositions, for which it was necessary to start with the theoretical weight of lanthanum carbonate hydrates having either four or five waters of hydration. *See* JA 4887-4888.

<sup>10</sup> Shire’s proposed constructions of the various iterations of the “water content” claim terms identified for construction by the parties in the ‘465 and ‘428 Patents are set forth on pages 23-24 of Shire’s opening brief.

**C. “Therapeutically Effective Amount” And “Amount Effective to Treat Hyperphosphatemia” (’428 Patent, Claim 1)**

<b>Term To Be Construed</b>	<b>Shire’s Proposal</b>	<b>Defendants’ Proposal</b>
<b>therapeutically effective amount</b>	amount or dose sufficient (i) to detectably decrease the serum phosphate levels of a subject or (ii) at a minimum, to keep the serum phosphate levels of a subject substantially constant	wherein the amount of $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ present in the composition is effective to treat hyperphosphatemia
<b>amount effective to treat hyperphosphatemia</b>	amount or dose of lanthanum carbonate sufficient (i) to detectably decrease the serum phosphate levels of a subject or (ii) at a minimum, to keep the serum phosphate levels of a subject substantially constant	wherein the amount of $\text{La}_2(\text{CO}_3)_3 \cdot x\text{H}_2\text{O}$ present in the composition is effective to treat hyperphosphatemia

There ought to be no dispute about the meaning of these claims terms. The specification expressly defines “therapeutically effective amount” as set forth in Shire’s proposed construction, and the parties agree that, as the intrinsic evidence demonstrates, “amount effective to treat hyperphosphatemia” carries the same meaning. *See* Pls. Br. at 31-32; Defs. Br. at 26; Brittain Decl. ¶ 80. Defendants’ expert even admits that Shire’s proposed constructions are “consistent” with how the specification defines the terms. Brittain Decl. ¶ 80.

In another transparent attempt to add extraneous limitations to the claims, however, Defendants ask the Court to disregard the specification’s express definition, in violation of the canons of construction. Defendants even make the bizarre accusation that Shire “fixate[s] on the specification’s definition of ‘therapeutically effective amount.’” Defs. Br. at 28. Of course Shire focuses on this explicit definition: “When a patentee explicitly defines a claim term in the patent specification, the patentee’s definition controls.” *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380 (Fed. Cir. 2009); *see also Phillips*, 415 F.3d at 1316 (“[T]he specification

may reveal a special definition given to a claim term . . . . In such cases, the inventor's lexicography governs.”).

Defendants purport to rely on the opinion of their expert (who has no experience treating hyperphosphatemia), *see* Defs. Br. at 27, but it is well established that when the specification explicitly defines a term, “extrinsic evidence is simply irrelevant.” *Martek*, 579 F.3d at 1382. That Defendants' expert does not agree with what he recognizes to be “the definitions set forth in the specification of the '428 patent for these terms,” Brittain Decl. ¶ 81, does not counsel for a different construction of the claim terms; it simply underscores how his opinions flout the canons of construction in order to support Defendants' desired positions and why his opinions ought therefore to be accorded little weight.

**D. “Stabilizing the Lanthanum Carbonate Against Substantial Decarboxylation To Lanthanum Hydroxycarbonate” ('428 Patent, Claims 1 and 7)**

<b>Term To Be Construed</b>	<b>Shire's Proposal</b>	<b>Defendants' Proposal</b>
<b>stabilizing the lanthanum carbonate against substantial decarboxylation to lanthanum hydroxycarbonate<sup>11</sup></b>	retarding the lanthanum carbonate from degrading into lanthanum hydroxycarbonate in an amount sufficient so that a skilled artisan detects lanthanum hydroxycarbonate through visual inspection of an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after it has been exposed to 60° C and 95% relative humidity for at least 7 days	stabilizing the lanthanum carbonate present in the composition such that no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate is detectable in an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after the composition has been exposed to 60° C and 95% relative humidity for at least 7 days, wherein lanthanum hydroxycarbonate is a species characterized by the four peaks identified by “HC” in the x-ray powder diffraction pattern appearing in Figure 13 for t = 7 days

<sup>11</sup> The parties have proposed substantively identical constructions for the term “the lanthanum carbonate being stabilized against substantial decarboxylation to lanthanum hydroxycarbonate” in Claims 1 and 7.

The parties appear to be in substantial agreement as to the construction of this term. *See* Pls. Br. at 25; Defs. Br. at 28-29. Their disagreement centers on Defendants' proposal to import a limitation from the specification by construing "lanthanum hydroxycarbonate" to mean "a species characterized by the four peaks identified by 'HC' in the x-ray powder diffraction pattern appearing in Figure 13 for t = 7 days." Defs. Br. at 30. Importing a limitation from the specification is improper under well established law. *See Voda*, 536 F.3d at 1320; *Phillips*, 415 F.3d at 1323. The term "lanthanum hydroxycarbonate" needs no construction. It is a known chemical entity with a known chemical formula, "LaOHCO<sub>3</sub>." *See* JA 6140.

Moreover, there is no basis to construe "lanthanum hydroxycarbonate" as the four peaks identified in Figure 13, as Defendants urge. Figure 13 is but one of several x-ray diffraction patterns where peaks characteristic of lanthanum hydroxycarbonate are reported to be visible. *See* Pls. Br. at 28; *see also* JA 27-28, JA 32-33, JA 38 (other figures of '428 Patent exhibiting one or more peaks labeled "HC" for lanthanum hydroxycarbonate). Defendants' assertion that use of Figure 13 is appropriate because it is an XRPD pattern for lanthanum hydroxycarbonate not in the presence of mono- or disaccharides cannot survive even the barest scrutiny. For example, Figures 3 and 4 of the '428 Patent also show stressing of lanthanum carbonate hydrates without any mono- or disaccharides.

Defendants also attempt to exclude from the scope of the claims "any lanthanum hydroxycarbonate impurity *initially present* in the lanthanum carbonate bulk drug substance used to form the composition." Brittain Decl. ¶ 90 (emphasis added). While there is no textual basis for such an exclusion, Shire does not view this disagreement as of significance.

## E. “Is Not Observed In” (’428 Patent, Claims 1 and 7)

Term To Be Construed	Shire’s Proposal	Defendants’ Proposal
<b>is not observed in</b>	is not detected through visual inspection by a skilled artisan of	<i>Defendants have stated they cannot construe this term</i>
<b>the amount of the monosaccharide or disaccharide is such that lanthanum hydroxycarbonate is not observed in an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after it has been exposed to 60° C and 95% relative humidity for at least 7 days</b>	the amount of the monosaccharide or disaccharide contained in a lanthanum carbonate composition is sufficient so that lanthanum hydroxycarbonate is not detected through visual inspection by a skilled artisan of x-ray powder diffraction patterns after the composition has been exposed to 60° C and 95% relative humidity for at least 7 days	the amount of the monosaccharide or disaccharide present in the lanthanum carbonate composition is such that no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate present in the composition is detectable in an x-ray powder diffraction (XRPD) pattern of the composition containing lanthanum carbonate and one or more monosaccharides or disaccharides after the composition has been exposed to 60° C and 95% relative humidity for at least 7 days

The parties’ disagreement about this term concerns the meaning of the limitation that lanthanum hydroxycarbonate “is not *observed* in an x-ray powder diffraction pattern.” Shire’s proposed construction provides the ordinary meaning of “observe,” which connotes visual inspection, consistent with the specification’s explanation that compositions were tested for the presence of lanthanum hydroxycarbonate by evaluating whether “HC [lanthanum hydroxycarbonate], was . . . *seen*,” JA 47 (’428 Patent, Col. 15:17 (emphasis added)), or “[n]o decarboxylation . . . was *seen*,” *id.* (’428 Patent, Col. 15:26-27, Col. 15:35-36, Col. 15:44-45, Col. 16:7-9). The specification includes other passages and figures teaching that lanthanum hydroxycarbonate is observed by visual inspection of an x-ray powder diffraction pattern. Pls. Br. at 29-30; Myerson Decl. ¶¶ 56-59; *see, e.g.*, JA 0027-38 (’428 Patent, Figs. 3-14). Moreover,

Defendants' expert concedes that "visual inspection is certainly one of the[] techniques" by which to observe the presence of hydroxycarbonate. Brittain Decl. ¶ 91.

Defendants propose, however, that the claim limitation be defined more vaguely as "no lanthanum hydroxycarbonate . . . is *detectable*" in an x-ray powder diffraction pattern. Def. Br. at 31-32. While they include an unspecified set of techniques, such as various computer algorithms, Brittain Decl. ¶ 91, *no* such techniques are mentioned or even suggested in the specification or prosecution history. Myerson Decl. ¶¶ 58-59. Because Defendants concede that the technique identified in the '428 Patent – visual examination by a skilled artisan – is satisfactory and the intrinsic record offers no basis to include other techniques, Shire's proposed construction should be adopted.

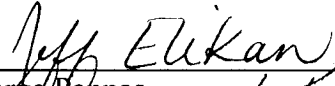
#### **IV. CONCLUSION**

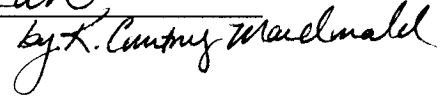
For the reasons set forth above and in Shire's opening brief, Shire respectfully requests that the Court adopt Shire's proposed constructions.

May 14, 2010

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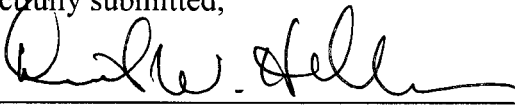
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